REMARKS

Summary of the Invention

The invention features a method for treating a patient suffering from aphthous by orally applying a composition consisting essentially of a topical anti-inflammatory steroid in combination with pentoxifylline (PTX) or thalidomide to the aphthous.

Summary of the Office Action

Claims 1-6 are pending. Claims 2, 5, and, in part, claims 4 and 6, are withdrawn from consideration for being directed to a non-elected invention. Claims 1, 3, 4, and 6 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. Claim 3 is rejected for lack of clarity. Claims 1, 3, 4, and 6 are rejected under 35 U.S.C. § 103 over Andrulis et al. (U.S. Patent No. 5,654,312; hereinafter "Andrulis") in combination with Quinn et al. (Stomatitis, Nov. 29, 1995; hereinafter "Quinn"). By this reply, Applicant withdraws claims 2 and 5, amends claims 1, 3, and 6, cancels claims 4, adds claims 7-12, and addresses each of the Examiner's rejections below.

Support for the Amendment

Support for the amendment to the specification is found in the specification as originally filed. Support for the amendment to claims 1 and 3, and for new claims 7-12, is found in the specification on page 2, lines 26-31, page 3, lines 10-25, and page 4, lines 1-6. Applicant also notes that the term "Decadron" in claim 3 has been replaced with the

generic name "dexamethasone" as Decadron is a trademark. No new matter is added by the amendment.

Rejection under 35 U.S.C. § 112, second paragraph

Claim 3 is rejected for lack of clarity for reciting "cyclosporin" in a Markush group of steroids. Claim 3 has been amended to remove the term "cyclosporin." This rejection should now be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph

Claims 1, 3, 4, and 6 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner states that the specification does not enable any person skilled in the art to use the invention commensurate in scope with the claims without undue experimentation because only a limited number of TNF alpha antagonist or steroid examples are set forth (Office Action, pp. 3 and 4). The Examiner acknowledges that the specification is enabling for the combination of dexamethasone or triamcinolone in combination with PTX or thalidomide (Office Action, p. 3).

In response to the Examiner's rejection, claim 1 has been amended to specify that the method of treating a patient suffering from aphthous comprises orally applying a composition that consists essentially of a topical anti-inflammatory steroid in combination with an inhibitor of TNF-α selected from PTX or thalidomide. Accordingly, a skilled artisan need only provide a topical anti-inflammatory steroid in combination with one of

the two TNF-α inhibitors identified in claim 1 to treat apthous in a patient in need thereof. While some experimentation might be necessary to identify a topical anti-inflammatory steroid that, when combined with one of the two TNF-α inhibitors, treats aphthous, this is clearly not a bar to patentability if the experimentation is simply routine, which it is in the present case.

In analyzing what constitutes undue experimentation, the MPEP (§ 2164.06) citing *In re Wands* (858 F.2d 731, 8 USPQ2d 1400 (Fed Cir. 1988)) states:

> The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. (Emphasis added)

The identification of topical anti-inflammatory steroids for use in the present invention would simply require routine experimentation as a skilled artisan at the time of filing of the present application would have been familiar with topical anti-inflammatory steroids and, using the teachings of the present specification, could have easily screened these topical anti-inflammatory steroids for their ability, in combination with PTX or thalidomide, to treat aphthous. Such screening could easily be accomplished using standard techniques and thus does not constitute undue experimentation. In support of Applicants contention that topical anti-inflammatory steroids were known to skilled artisans and could be selected based on their anti-inflammatory activity, Applicants direct the Examiner to Boris and Hurley (J. Invest. Dermatol. 68:161-164, 1977; provided herewith as Exhibit A), which not only provides a list of topical anti-inflammatory

steroids, including, e.g., dexamethasone, hydrocortisone, prednisolone, triamcinolone, betamethasone, fluromethasone, paramethasone acetate, fluocinolone acetonide, fluocinonide, and flurandrene, but also provides an assay system that a skilled artisan could use to routinely identify topical steroids with anti-inflammatory activity for use in the present invention (see, e.g., page 163, col. 1, lines 21-25, of Boris and Hurley). Therefore, a skilled artisan, using the specification as filed and knowledge of topical anti-inflammatory steroids at the time of filing, as exemplified by Boris and Hurley, could have easily identified a topical anti-inflammatory steroid for use in the invention of present claims 1-12 without undue experimentation. Accordingly, Applicant respectfully requests that the rejection of claims 1, 3, 4, and 6 under 35 U.S.C. § 112, first paragraph, be withdrawn.

Rejection under 35 U.S.C. § 103(a)

Claims 1, 3, 4, and 6 are rejected under 35 U.S.C. § 103(a) over Andrulis in combination with Quinn. The Examiner states that it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ TNF antagonists and steroids in the treatment of aphthae because:

> Andrulis et al....teaches that TNF alpha antagonists (PTX and thalidomide) and dexamethasone (glucocorticoids/ corticosteroids) are useful in treating dermatoses with an autoimmune or inflammatory basis...[and] Quinn et al. teaches that aphthae is cause [sic] by an underlying autoimmune mechanism. (Office Action, p. 5)

Applicant respectfully traverses this rejection.

The M.P.E.P. § 2143 states:

> To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed.Cir.1991). (Emphasis Added)

Claim 1, as presently amended, recites a method of treating a patient suffering from aphthous by orally applying to the patient a composition consisting essentially of a topical anti-inflammatory steroid in combination with an inhibitor of TNF-α selected from PTX or thalidomide. The Examiner states that "Andrulis teaches [that] topically applied corticosteroids are useful in treating dermatoses with an autoimmune or inflammatory basis...[and] that both corticosteroids and thalidomide are known to be applied to the effected site topically in ointment form." (Office Action, p. 5) Andrulis, though, fails to disclose an orally-applied composition for use in treating aphthous that consists of the steroid/TNF-α antagonist combination presently recited in claim 1. The Examiner acknowledges this by stating that "Andrulis...does not particularly teach a method of treating oral ulcerations or apthae." (Office Action, p. 5; emphasis added). Therefore, Andrulis fails to teach or suggest all of the limitations of present claim 1, and claims dependent therefrom.

Quinn fails to remedy the deficiencies of Andrulis. The Examiner states that "Quinn...teaches that aphthae is cause [sic] by an underlying autoimmune mechanism." (Office Action, p. 4). Quinn, like Andrulis, fails to teach or suggest a composition for treating aphthous that consists of a topical anti-inflammatory steroid in combination with an inhibitor of TNF-α selected from PTX or thalidomide, or that such a composition is administered by oral application. Because neither Andrulis nor Quinn, either solely or in combination, teaches or suggests the oral administration of a composition consisting essentially of a topical anti-inflammatory steroid in combination with an inhibitor of TNF-α selected from PTX or thalidomide for the treatment of aphthous, these references fail to serve as the basis for a *prima facie* case of obviousness (see M.P.E.P. § 2143, *supra*). Accordingly, Applicant respectfully requests that the rejection of claims 1, 3, 4, and 6 under 35 U.S.C. § 103(a) be withdrawn.

CONCLUSION

Applicant submits that the claims are in condition for allowance, and such action is respectfully requested.

A check for the required fee under 37 C.F.R. § 1.17(e) for the Request for Continued Examination is enclosed. Also enclosed, is a petition to extend the period for replying for two months, to and including January 26, 2004, as January 24, 2004 falls on a Saturday, and a check for the required fee under 37 C.F.R. § 1.17(a). If there are any other charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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